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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/399,120	09/20/1999	DESMOND MASCARENHAS	220952029300	1886

7590 09/24/2003

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EXAMINER
GUPTA, ANISH

ART UNIT	PAPER NUMBER
1654	27

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/399,120	MASCARENHAS, DESMOND	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,16 and 18-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7-7-03 has been entered.

1. The amendment filed, 7-23-03 is hereby acknowledged. The amendment added claims 45 47. Claims 1-47, are pending in the application.

1. Applicant's election without traverse of Group I, claims 1-10 and 16 in Paper No. 8 is acknowledged. Claims 11-15, 17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 8. Newly added claims, 45-47, have been placed in Group I and thus have been examined along with claims 1-10, 16 and 18-47.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112
First Paragraph

3. Claims 1-10, 16 remain and newly added claims 18-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous office action and the reasons set forth below.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Applicants argue that in the advisory action, only part of the definition of Null IGF has been quoted. The specification also recites that a "[n]ull IGF-1 retains its ability to bind IGFBP-3, but is altered in its receptor binding and/or activating properties." Thus, the genus is much smaller than 70 to the 20th power. Applicants also state that the Applicants have not broadened the meaning of "null IGF" beyond that which is consistent with its ordinary meaning.

Applicant's arguments filed 7-7-03 have been fully considered but they are not persuasive. .

First, it is unclear as to the "ordinary meaning" of Null IGF. Structurally speaking, it is unclear what modification in the IGF would render an IGF molecule a "null IGF." A search on Chemical abstracts, the patent database, the international patent database, and other scientific journal database, for the term "null IGF" leads to five references. Three of these five references utilize Applicants definition. The other two identify the receptor rather than the "null IGF" molecule. Thus, in light of the art, the most concise meaning is as indicated in the advisory action.

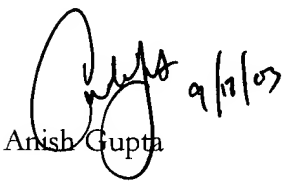
Further, Applicants state that the meaning is more than just any substitution but is also a function limitation. However, one of ordinary skill in the does not readily know which modification would lead to the desired functional activity. In essence the functional definition does not provide any guidance as to the structural definition of the Null IGF. One would have to make the analog, then determine if it has the binding activity. The fact remains that null IGF can be any amino acid substitution in the IGF and the genus is as broad as indicated in the previous office action. If the genus is small, as Applicants contend, then Applicants are requested to furnish references that indicate the "ordinary meaning" of null IGF and which clearly establishes that null IGF is a class of compounds within the IGF family.

As a note, references with regards to animal models have now been applied. A more thorough explanation of why animal models are ineffective in predicting cancer.
Dermer states that "immunotherapy's killing power of the transformation of 3T3 cells by a mutated protooncogene, simply does not have the same significance for cells in vivo.' (See page 320). Further, "[t]he facts indicate, however, that petri dish cancer is really poor representation of malignancy, with characteristics profoundly different from human disease." (See page 320). Similar sentiments are echoed in a Science article by Trisha Gura. The article indicates that the fundamental problem in cancer research is that model systems are not predictive of in-vivo activity (see page 1041). The article goes on to state xenograft models in mice "don't behave like naturally occurring tumors in humans--they don't spread to other tissues." (See page 1041). Further, other systems such as clonogenic assays are not always helpful since they "can't always predict how a tumor will respond to a drug in an animal" and "[s]ometimes they don't work because the cells simply fail to divide n culture." (See page 1042). In essence, the art indicates that "rodents are better predictors of human reaction to cardiovascular or anti-inflammatory agents than cancer or diseases of the central nervous system." (See Time article by Frederic Golden on page 44). Further, the Jain article states that for solid tumors, the clinical results to date have not met the high

expectation obtained as a result of in in-vitro testing (see the paragraph of page 1079-1080). "Even with the best animal model, however, we still need to better understand how the process of biodistribution of various agents 'scales-up' from mouse to human. The biochemical and physiological differences between these species make this knowledge critical." Thus, the cancer animal models and cell models, although provide valuable information for delivery of therapeutics, to not correlate to human in-vivo efficacy. For these reasons and the reasns set forth in the previous office actions, the rejeciton is maintained.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda , can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Anish Gupta